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## Redox-Sensitive Liposomes for Glioblastoma Treatment

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**Hypothesis/aim:** Treatment of glioblastoma remains a challenge due to inability of the drug to reach the intracellular target. Invasive glioblastoma is associated with high grade vascularization and break-down of the blood-brain barrier (BBB), which could aid in delivering drugs to the tumor site. However, once at the tumor site, the drug has to be internalized and transported to the specific target. The aim of the current project is to develop a drug delivery system (DDS) that crosses the permeable BBB to specifically target invasive glioblastoma cells and thereby facilitate uptake. Furthermore the DDS will be intracellularly activated to escape the endosome and drug efflux mechanism, thereby transporting the drug to the intracellular target. The DDS consists of a positively charged unsaturated liposome formulation, redox-sensitive lipopeptides with a PEG-linker that shields the positive charge, and a cell-penetrating or targeting moiety. Doxorubicin is encapsulated within the liposome lumen.

**Methods:** Redox-sensitive liposomes are prepared by post-insertion of lipopeptides containing a disulphide bridge into positively charged liposomes. Reduction of the disulphide is confirmed by HPLC and zeta-potential (charge-reversal) measurements. Uptake in U87 cells is confirmed by flow cytometry. Toxicity of the liposomes is investigated by MTS assay. Intracellular transport and distribution is investigated by confocal microscopy.

**Results:** Cleavage and charge-reversal has been confirmed for two different formulations. Uptake experiments show that the DDS is indeed taken up by glioblastoma cells when a cell penetrating moiety is included in the formulation. Furthermore, uptake is confirmed upon activation (charge-reversal) by cleavage of the disulphide bridge.